

Advantages of adding a course of tetracycline to single dose ampicillin and probenecid in the treatment of gonorrhoea

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SUMMARY *Chlamydia trachomatis* was reisolated from 11 of 12 men with gonorrhoea who had initially yielded chlamydiae and who had been treated with ampicillin and probenecid (AMP) only, but from none of five such men treated with ampicillin and probenecid followed by tetracycline (AMPT). These results correlated with the absence of postgonococcal urethritis (PGU) in the group treated with AMPT. *C. trachomatis* was isolated or reisolated from 20 of 25 women after treatment with AMP, compared with none of 14 women treated with AMPT. We recommend the addition of a course of tetracycline to the routine single dose treatment for gonorrhoea in men and women.

Introduction

The combination of ampicillin and probenecid in single dosage is widely used for the treatment of uncomplicated gonorrhoea. Oral ampicillin in a dose of 2 g, plus oral probenecid (1 g) has been successfully used in both men and women attending the department of genitourinary medicine of this hospital for many years. In 1976 we reported that this regimen failed to eradicate concurrent infections with *Chlamydia trachomatis* in either sex.¹ Since that time we have modified the regimen to include 500 mg oxytetracycline orally every six hours for seven days, starting 24 hours after the single dose of ampicillin and probenecid. We report here an analysis of the patients treated in 1976 with ampicillin and probenecid (AMP) and patients treated in 1981 with ampicillin and probenecid followed by a course of oxytetracycline (AMPT).

Patients and methods

Specimens were collected from patients as follows.

MEN

A specimen of urethral secretion was taken with a disposable plastic loop and spread on a slide for

Gram staining and microscopy. A second specimen was inoculated on to a culture plate for isolation of *Neisseria gonorrhoeae*. A wire mounted, cotton wool tipped endourethral swab was then inserted 4-5 cm into the urethra, and on removal placed into transport medium for chlamydial culture.

WOMEN

The urethra and cervix were cleaned with gauze, then specimens were taken with plastic loops for microscopy and culture for *N. gonorrhoeae*. A specimen for chlamydial culture was then taken using a cotton wool tipped swab inserted into the cervical canal. The swab was broken off into a chlamydial transport medium.

DIAGNOSIS AND TREATMENT

A provisional diagnosis of gonorrhoea was based on the presence of characteristic intracellular Gram negative diplococci and was confirmed by isolation of *N. gonorrhoeae* in all cases. After a provisional or confirmed diagnosis of gonorrhoea men and women in 1976 were given a single oral dose of 2 g ampicillin plus 1 g probenecid (AMP) in the clinic. In addition to the above treatment men and women diagnosed in 1981 received oxytetracycline 500 mg orally every six hours for seven days, starting the day after they received the ampicillin and probenecid. Patients were followed up for two weeks after treatment, with at least two re-examinations and laboratory tests as described below. Patients were advised to abstain from sexual intercourse during this period.

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TABLE I Effect of treatment with AMP or AMPT on the isolation of *C trachomatis* and the development of PGU in 91 men with gonococcal urethritis

Isolate obtained:		Treatment with AMP (n = 46):		Treatment with AMPT (n = 45):	
Before treatment	After treatment	No treated	No developed PGU	No treated	No developed PGU
Yes	Yes	11	10	0	0
Yes	No	1	1	5	0
No	Yes	3	1	0	0
No	No	31	5	40	9

AMP = ampicillin and probenecid; AMPT = ampicillin, probenecid, and tetracycline; PGU = postgonococcal urethritis.

LABORATORY METHODS

Cultures for *N gonorrhoeae* were performed using a modified Thayer-Martin medium.² Cell culture for *C trachomatis* was performed using McCoy cells treated with idoxuridine (IUDR) as described previously.³ Post gonococcal urethritis (PGU) was diagnosed in men from whom *N gonorrhoeae* was not isolated, who had 10 or more polymorphonuclear leucocytes in a Gram stained smear of a urethral specimen examined at a magnification of $\times 900$, or had more than 15 polymorphonuclear leucocytes per high power field in a centrifuged deposit of first catch urine.

STATISTICAL ANALYSIS

Statistical correlates were calculated using χ^2 test with Yates' correction.

Results

Table I shows that 46 men with confirmed gonococcal urethritis were treated with AMP, and *C trachomatis* was isolated from the urethra of 12 (26%) before treatment; 45 were treated with AMPT, and *C trachomatis* was isolated from the urethra of five (11%) before treatment. Although this difference in isolation of *C trachomatis* from the two groups was not significant ($\chi^2 = 2.44$; $p > 0.1$), it was noted that the group treated with AMPT contained a higher proportion of homosexual men (17 (38%)) than the group treated with AMP (3 (7%)). *C trachomatis* was not isolated from the urethra of any homosexual men.

N gonorrhoeae was not reisolated during follow up in any of the men in either treatment group. *C trachomatis* was reisolated from 11 of 12 patients in the group treated with AMP, but from none of five in the group treated with AMPT; the difference was significant ($\chi^2 = 9.28$; $p < 0.01$). Furthermore, chlamydiae were isolated for the first time three weeks or more after treatment in three of 46 men treated with AMP, but in none of 45 treated with AMPT.

PGU was diagnosed in 17 (37%) of 46 patients in the group treated with AMP and in nine (20%) of 45 in the group treated with AMPT. The difference was not significant ($\chi^2 = 2.43$; $p > 0.5$). Of the 12 patients treated with AMP who initially yielded chlamydiae, however, 11 (92%) developed PGU compared with none of the five treated with AMPT. The difference was significant ($\chi^2 = 6.97$, $p < 0.01$). The addition of tetracycline to the treatment regimen had no significant effect on the development of PGU in patients who did not initially yield chlamydiae ($\chi^2 = 0.01$; $p > 0.5$).

Table II shows that 44 women with cervical gonorrhoea were treated with AMP, and *C trachomatis* was isolated from 23 (52%) before treatment; 40 were treated with AMPT, and *C trachomatis* was isolated from the cervix of 14 (35%). The difference in isolation rates between the two groups was not significant ($\chi^2 = 1.88$; $p > 0.1$).

TABLE II Effect of treatment with AMP or AMPT on isolation of *C trachomatis* in 84 women with gonorrhoea

Isolate obtained:			
Before treatment	After treatment	No treated with AMP (n = 44)	No treated with AMPT (n = 40)
Yes	Yes	18	0
Yes	No	5	14
No	Yes	2	0
No	No	19	26

AMP = ampicillin and probenecid; AMPT = ampicillin, probenecid, and tetracycline.

C trachomatis was reisolated from 18 (78%) of the 23 women initially positive in the group treated with AMP, compared with none of the 14 patients in the group treated with AMPT. This difference was highly significant ($\chi^2 = 17.54$; $p < 0.001$). In addition, two patients in the group treated with AMP who did not initially yield chlamydiae, yielded isolates after treatment, but no patient yielded isolates after treatment with AMPT.

Discussion

In men AMPT eradicated *C trachomatis* from the urethra, and failure to reisolate *C trachomatis* after treatment with AMPT correlated with the absence of PGU in these patients. In the female patients AMPT was also successful in eradicating *C trachomatis* from the cervix.

Until chlamydial diagnostic services become more widely available, we think it is essential to recognise the possibility of concurrent infection with chlamydiae in patients with gonococcal infection. We do not advocate the use of tetracyclines alone to treat gonorrhoea and chlamydial infection. Gonococcal resistance to tetracycline is not uncommon,⁴ and this would preclude the use of a tetracycline in the absence of sensitivity testing. On the other hand, *C trachomatis* shows no resistance to tetracycline. The use of a course of tetracycline after standard single

dose antigonococcal treatment has the important advantage of allowing flexibility of choice of the agent to be used against the gonococcal infection (determined by local patterns of resistance including the prevalence of β -lactamase producing strains) while curing the concurrent chlamydial infection.

References

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